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## **DEPARTMENT OF HEALTH AND HUMAN SERVICES**

### **National Institutes of Health**

#### **Government-Owned Inventions; Availability for Licensing**

**AGENCY:** National Institutes of Health, HHS

**ACTION:** Notice

**SUMMARY:** The inventions listed below are owned by an agency of the U.S.

Government and are available for licensing in the U.S. in accordance with 35 U.S.C. 209 and 37 CFR Part 404 to achieve expeditious commercialization of results of federally-funded research and development. Foreign patent applications are filed on selected inventions to extend market coverage for companies and may also be available for licensing.

**FOR FURTHER INFORMATION:** Licensing information and copies of the U.S. patent applications listed below may be obtained by writing to the indicated licensing contact at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852-3804; telephone: 301-496-7057; fax: 301-402-0220. A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

**SUPPLEMENTARY INFORMATION:** Technology descriptions follow.

### **Resolution Enhancement Technique for Light Sheet Microscopy Systems**

**Description of Technology:** The invention pertains to a technique for enhancing the resolution of a light sheet microscopy technique by adding an additional enhanced depth-of-focus optical arrangement and high numerical aperture objective lens. The technique employs an arrangement of three objective lenses and a processor for combining captured images from the objectives. The resulting image composite retains the greater resolving power of the third high numerical aperture objective lens by imaging the light sheet with the third objective lens and enhanced depth-of-focus arrangement so that the overall resolution of the light sheet system is improved. The depth of field arrangement could be a simple oscillation of the third objective, or a “layer cake” or cubic phase mask component. Any loss in lateral resolution that results from the depth of field arrangement may be compensated for by deconvolution. In some embodiments, other optics, such as an axicon or annular aperture, can provide extended depth of field.

**Potential Commercial Applications:** Resolution enhancement in light microscopy

**Competitive Advantages:** Image composition using processing system

**Development Stage:**

- Early-stage
- Prototype

**Inventors:** Hari Shroff (NIBIB), Yicong Wu (NIBIB), Sara Abrahamsson (The Rockefeller University)

**Intellectual Property:** HHS Reference No. E-232-2014/0 - US Provisional Patent Application 62/054,484 filed September 24, 2014

**Related Technology:** HHS Reference No. E-078-2011/0 -

- PCT Application No. PCT/US2012/27524 filed March 02, 2012
- US Patent Application No. 14/003,380 filed September 5, 2013, which published as US 2014-0126046-A1 on May 08, 2014

**Licensing Contact:** Michael Shmilovich, Esq.; 301-435-5019;  
[shmilovm@mail.nih.gov](mailto:shmilovm@mail.nih.gov)

**Collaborative Research Opportunity:** The National Institute of Biomedical Imaging and Bioengineering is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize light sheet microscopy image resolution enhancement. For collaboration opportunities, please contact Cecilia Pazman at 301-594-4273 or [pazmance@nhlbi.nih.gov](mailto:pazmance@nhlbi.nih.gov).

## **Resolution Enhancement for Line-Scanning Excitation Microscopy**

**Description of Technology:** The invention describes a method for improving the spatial resolution of optical microscopes that use line-scanning excitation, such as line-scanning confocal microscopes, line-scanning STED microscopes, or line-scanning light-sheet microscopes. Common elements of the invention include: a) an apparatus for exciting and scanning a line-like excitation focus through the sample; b) an optical arrangement on the detection side of the microscope for manipulating the spacing and/or

width of the resulting fluorescence emissions; c) integration and optional post-processing of the manipulated fluorescence emissions after capture by an area detector such as a camera. The resolution increase may be performed with no or marginal decrease in temporal resolution relative to the conventional line-scanning microscopes upon which the technique is based.

**Potential Commercial Applications:** Fluorescence microscopy

**Competitive Advantages:**

- Improved resolution
- Enhanced acquisition speed relative to other forms of super-resolution

microscopy

**Development Stage:** Prototype

**Inventors:** Hari Shroff, Andrew York, John Giannini, Abhishek Kumar (all of NIBIB)

**Intellectual Property:** HHS Reference No. E-225-2014 - US Provisional Patent Application 62/054,481 filed September 24, 2014

**Licensing Contact:** Michael Shmilovich, Esq.; 301-435-5019;

[shmilovm@mail.nih.gov](mailto:shmilovm@mail.nih.gov)

**Collaborative Research Opportunity:** The National Institute of Biomedical Imaging and Bioengineering is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize fluorescent microscopy. For collaboration opportunities, please contact Cecilia Pazman at 301-594-4273 or [pazmance@nhlbi.nih.gov](mailto:pazmance@nhlbi.nih.gov).

## **Chemotherapeutic Anti-cancer Agents**

**Description of Technology:** Available for licensing are new compounds derived from 4-benzyl-amino-benzyl alcohol. These compounds possess potent activity in multiple *in vitro* models of cancer cell growth inhibition and *in vivo* xenograft models of renal tumor regression. These compounds could potentially be developed into promising therapeutic agents for the treatment of various cancers.

**Potential Commercial Applications:** Chemotherapy of cancer

**Competitive Advantages:**

- Extreme potency for tumor regression *in vivo*.
- Compounds with similar profiles have been approved by the FDA as chemotherapeutic agents.

- Preliminary toxicology data available.

**Development Stage:**

- In vitro data available
- In vivo data available (animal)

**Inventors:** Joel Morris and Donn Wishka (NCI)

**Intellectual Property:** HHS Reference No. E-027-2014/0 - US Application No. 61/933,606 filed 20 Jan 2014

**Licensing Contact:** Patrick McCue, Ph.D.; 301-435-5560;

[mccuepat@od.nih.gov](mailto:mccuepat@od.nih.gov)

## **Novel Codon-Optimized Gene Therapeutic for Methylmalonic Acidemia**

**Description of Technology:** Methylmalonic Acidemia (MMA) is a metabolic disorder characterized by increased acidity in the blood and tissues due to toxic accumulation of protein and fat by-products resulting in seizures, strokes, and chronic kidney failure. A significant portion of MMA cases stem from a deficiency in a key mitochondrial enzyme, methylmalonyl-CoA mutase (*MUT*), required to break down amino acids and lipids. Currently, there are no treatments for MMA and the disease is managed primarily with dietary restriction of amino acid precursors and liver-kidney transplantation in severe cases.

The present invention describes a synthetic codon-optimized *MUT* gene (co-*MUT*) that improves expression of human methylmalonyl-CoA mutase. A series of novel gene therapy vectors containing co-*MUT* rescued MMA mice from lethality and lowered levels of methylmalonic acid in the blood. Results of pre-clinical efficacy studies demonstrate a promising therapy for MMA and other renal-associated disorders.

**Potential Commercial Applications:**

- The co-*MUT* transgene could be used to treat MMA patients.
- In addition, it could be used to produce *MUT* in vitro for MMA enzyme replacement therapy.

**Competitive Advantages:** co-*MUT* transgene could be used through non-viral and viral gene delivery.

**Development Stage:**

- In vitro data available
- In vivo data available (animal)

**Inventors:** Charles P. Venditti and Randy J. Chandler (NHGRI)

**Intellectual Property:** HHS Reference No. E-243-2012/0 -

- US Provisional Application No. 61/792,081 filed 15 March 2013
- PCT Application No. PCT/US2014/028045 filed 14 March 2014

**Licensing Contact:** Vince Contreras, Ph.D.; 301-435-4711;

[vince.contreras@nih.gov](mailto:vince.contreras@nih.gov)

**Collaborative Research Opportunity:** The Organic Acid Research Section at the National Human Genome Research Institute is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize codon-optimized MUT constructs. For collaboration opportunities, please contact Claire T. Driscoll at [cdriscoll@mail.nih.gov](mailto:cdriscoll@mail.nih.gov).

Dated: October 28, 2014

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Richard U. Rodriguez, M.B.A.  
Acting Director  
Office of Technology Transfer  
National Institutes of Health

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